II. REMARKS

Formal Matters

Claims 1, 5, 7, 14, and 20-22 are pending after entry of the amendments set forth herein.

Claims 1, 3, 5, 7, 14, 15, and 20-22 were examined and were rejected.

Claims 1 and 14 are amended. The amendments to the claims were made solely in the interest of expediting prosecution, and are not to be construed as acquiescence to any objection or rejection of any claim. Support for the amendments to claims 1 and 14 is found in the claims as originally filed, and throughout the specification, in particular at the following exemplary locations: claim 1: paragraph 0071; and claim 14: paragraphs 0028, 0050, 00109, and 00127. Accordingly, no new matter is added by these amendments.

Claims 3 and 15 are canceled without prejudice to renewal, without intent to acquiesce to any rejection, and without intent to surrender any subject matter encompassed by the canceled claims. Applicants expressly reserve the right to pursue any canceled subject matter in one or more continuation and/or divisional applications.

Applicants respectfully request reconsideration of the application in view of the remarks made herein.

Rejection under 35 U.S.C.§112, first paragraph

Claims 1, 3, 5, 7, 14, 15, and 20-22 were rejected under 35 U.S.C.§112, first paragraph, as allegedly lacking enablement.

The Office Action stated that the specification is enabling for: a) a transgenic mouse whose genome comprises a homozygous modification of the endogenous apoE allele, wherein the modified apoE allele comprises an apoE-encoding nucleic acid under transcriptional control of endogenous regulatory sequences, wherein the modified apoE allele encodes a modified apoE polypeptide that exhibits domain interaction characteristic of human apoE4, wherein the modified endogenous mouse apoE polypeptide comprises a Thr to Arg substitution at a position equivalent to amino acid 61 of human apoE4, wherein the modified apoE polypeptide exhibits preferential binding to LDL, and wherein the mouse exhibits apoE4-related neurodegeneration; b) cell isolated from the mouse; and c) a method of identifying an agent that reduces a phenomenon associated with apoE4-related neurodegeneration by contacting the mouse with a test agent, and determining the effect of the test agent on reducing the apoE4-related neurodegeneration. The Office Action stated that the specification does

not reasonably provide enablement for the breadth of the mice, including homozygous and heterozygous, and methods of using these mice in methods of identifying an agent that reduces a phenomenon associated with Alzheimer's Disease. Applicants respectfully traverse the rejection.

The instant specification provides enablement for a claimed gene-targeted mouse, where the gene-targeted mouse is heterozygous or homozygous for the modified apoE allele.

The specification states that the present invention provides gene-targeted animals that comprise a genetic modification in one or both alleles of the endogenous apoE gene. Specification, paragraph 0018. The specification provides ample description as to how to determine whether a modified apoE polypeptide encoded by the modified apoE allele in the gene-targeted animal exhibits preferential binding to lower density lipoproteins (LDL), and whether the gene-targeted animal exhibits apoE4-related neurodegeneration. For example, whether a modified apoE polypeptide encoded by the modified apoE allele in the gene-targeted animal exhibits preferential binding to LDL can be determined using an emulsion binding assay. Specification, paragraph 00133. Whether a modified apoE polypeptide encoded by the modified apoE allele in the gene-targeted animal exhibits preferential binding to LDL can be determined using an assay as described in the working example. Specification, paragraphs 00191-00194. Whether the gene-targeted animal exhibits apoE4-related neurodegeneration can be determined by assaying behavior, by histochemical analysis, and the like. Specification, paragraphs 00124, 00128-00130; paragraphs 00135-00136; and paragraphs 00144-00147. Accordingly, the instant specification provides ample enablement for the gene-targeted mouse as claimed.

The instant specification provides ample enablement for a method of identifying an agent that reduces a phenomenon associated with AD.

The instant specification states that a subject gene-targeted animal (e.g., an animal as recited in claim 1) is useful for identifying agents that reduce a phenomenon associated with AD. Specification, page 8, paragraph 0029; and paragraph 00196. The specification states that phenomena associated with AD include neuropathological developments. Specification, paragraph 0046. Such neuropathological developments include neurodegeneration. Specification, paragraph 00127; and paragraph 00128. The specification describes how to determine whether a test agent reduces a phenomenon associated with AD. Specification, paragraphs 00128-00130. Accordingly the specification provides adequate enablement for claims 14 and 15.

Nevertheless, and solely in the interest of expediting prosecution, claim 1 is amended to recite "wherein the gene-targeted mouse is homozygous for the modified apoE allele"; and claim 14 is amended to recite a "method of identifying an agent that reduces apoE4-related neurodegeneration."

Applicants submit that the rejection of claims 1, 3, 5, 7, 14, 15, and 20-22 under 35 U.S.C. §112, first paragraph, has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

III. CONCLUSION

Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number UCAL-222.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: August 9, 2005

By: _____
Paula A. Borden
Registration No. 42,344

BOZICEVIC, FIELD & FRANCIS LLP
1900 University Avenue, Suite 200
East Palo Alto, CA 94303
Telephone: (650) 327-3400
Facsimile: (650) 327-3231

F:\DOCUMENT\UCAL\222\resp 05-17-05 OA.doc